

REMARKS

Claims 60, 65-71, 76-83, 88-96, 101-117, 126-157 are currently pending and presented for examination. Claims 1-59, 61-64, 72-75, 84-87, 97-100 and 118-125 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of any or all of these canceled claims in one or more continuing applications.

Claims 60 and 89 are amended. Claim 60 is amended to add the inadvertently omitted term "location" from the phrase "second assay location." Claim 89 is amended to delete the term "first" from the phrase "first bioactive agent." None of these amendments constitute new matter.

Claims 142-157 are new. Support for these new claims can be found throughout the specification as originally filed. For example, support for claims 142-157 can be found at page 2, line 36 to page 3, line 8; page 9, line 35 to page 10, line 24; page 19, line 12-21; page 35, lines 4-10; and page 36, lines 10-27. None of these new claims constitute new matter.

After having carefully reviewed the instant Office Action, Applicants respectfully traverse the Examiner's rejections set forth therein.

Rejection of claims 60, 66-71, 77-83, 89-96, 103, 104, 106-117, 127, 129 and 131-141 under 35 U.S.C. § 103(a)

The Examiner rejects claims 60, 66-71, 77-83, 89-96, 103, 104, 106-117, 127, 129 and 131-141 as allegedly obvious over US Patent No. 6,327,410 (Walt et al.) in view of US Patent No. 6,680,206 (McDevitt et al.) and/or US Patent No. 7,041,510 (Seul et al.). In particular, the Examiner asserts that Walt et al. disclose an array and methods of making an array having spatially identifiable first and second assay locations on a surface with microspheres randomly placed in depressions within the assay location. Furthermore, the Examiner alleges that blank beads were known in the art and a skilled artisan would have added them to the arrays disclosed by Walt et al. Specifically, the Examiner asserts that both McDevitt et al. and Seul et al. disclose the use of blank beads in arrays. The Examiner then contends that a skilled artisan would have been motivated to combine, with a reasonable expectation of success, the disclosures of either McDevitt et al. or Seul et al. with that of Walt et al. in order to arrive at the subject matter of the above-rejected claims. In particular, the Examiner alleges that a skilled artisan would have

derived the benefit of enhanced optical analysis allowing simultaneous evaluation of multiple chemically distinct analytes.

As discussed in their previous response filed August 27, 2009, Applicants maintain that each of the above-rejected claims is not obvious over any combination of Walt et al., McDevitt et al. and/or Seul et al. The Examiner's response to Applicant's arguments in item 5 of the instant Office Action succinctly clarifies the three allegations of obviousness that remain to be resolved in connection with the currently-pending claim set. Applicants understand the three allegations of obviousness to be as follows:

1) The Examiner asserts that the above-rejected claims (including independent claims 60, 71, 83 and 94) are obvious over the combination of Walt et al. and McDevitt et al.

2) The Examiner asserts that the above-rejected claims (including independent claims 60, 71, 83 and 94) are obvious over the combination of Walt et al. and Seul et al.

3) The Examiner asserts that dependent claims that recite either "said second plurality of depressions have microspheres from said first population of microspheres and said second population of microspheres associated therewith" (for example, dependent claims 95, 112, 114 and 116) or "said first plurality of depressions have microspheres from said first population of microspheres and said second population of microspheres associated therewith" (for example, dependent claims 96, 113, 114 and 117) are also obvious over the combination of Walt et al. and McDevitt et al., the combination of Walt et al. and Seul et al. or a combination of all three of these references.

First allegation of obviousness

In connection with the first allegation of obviousness, Applicants argued in their response filed August 27, 2009 that the combination of Walt et al. and McDevitt et al. does not teach or suggest, among other things, the random distribution of blank microspheres at the first and second assay locations as recited by the above-rejected claims. In particular, Applicants argued that the blank microspheres described by McDevitt et al. were used as negative controls in a specific assay, and thus, the location of the blank microspheres must have been known. In the instant final Office Action, the Examiner responded to Applicants' arguments as follows:

Applicant argues that the cited art does not teach random distribution of blank microspheres. Applicant acknowledges that McDevitt uses blank microspheres but asserts that "It is clear from Example 2 and Figure 16 of the McDevitt et al reference that the blank microspheres as well as each of the differently derivatized microspheres were positioned on the array such that their locations were known". The assertion is noted. However, it is unclear to the examiner how the cited teachings illustrate known locations. Figure 16 is a chart listing color response for beads in various solutions and Example 2 is silent regarding known location. Furthermore, McDevitt specifically teaches randomly placed microsphere populations (Column 10, lines 13-16). Therefore, Applicant's assertions of known locations are not persuasive (see instant Office Action at page 8).

Applicants have carefully considered the Examiner's response. Nevertheless, Applicants maintain the position that the combination of Walt et al. and McDevitt et al. does not teach or suggest the random distribution of blank microspheres at the first and second assay locations as recited by the above-rejected claims. The Examiner states that it is not clear how the disclosure at Figure 16 and Example 2 of McDevitt et al. teach known locations. Furthermore, the Examiner argues that McDevitt et al. "specifically teach randomly placed microsphere populations" at column 10, lines 13-16. The entire paragraph appearing at column 10, lines 9-16 of McDevitt et al. is reproduced as follows:

When forming an array which includes a plurality of particles, the particles may be placed in the array in an ordered fashion using the micromanipulator. In this manner, a (sic) ordered array having a predefined configuration of particles may be formed. Alternatively, the particles may be randomly placed within the cavities. The array may subsequently undergo a calibration test to determine the identity of the particle at any specified location in the supporting member (see McDevitt et al. at column 10, lines 9-16).

While McDevitt et al. state that “the particles may be randomly placed within the cavities,” McDevitt et al. do not state that blank particles should be treated this way. In fact, McDevitt et al. also disclose that particles can be placed on an array in “an ordered fashion” so as to form an array having “a predefined configuration of particles” (see McDevitt et al. at column 10, lines 10-13). Thus, not all particles are randomly distributed on the array.

As discussed in Applicants’ response of August 27, 2009, McDevitt et al. describe only the use of blank particles as negative controls in assays conducted on a particle array. Applicants citations to Figure 16 and Example 2 in their previous response were provided in order to focus on the two disclosures by McDevitt et al. that were alleged by the Examiner to constitute the use of randomly distributed blank particles in arrays (see Examiner’s allegations of obviousness at page 4 of the Office Action issued February 27, 2009, citing Fig. 16 and column 25, lines 1-45, both of which are contained within Example 2 of McDevitt et al., for allegedly teaching the use of blank microspheres. These allegations are maintained in the instant Office Action at page 3). As can be seen from the text of Example 2 (column 24, line 31 to column 25, line 59) of McDevitt et al., Figure 16, which depicts the results of the solid phase assays described in Example 2, and the Examiner’s own assessment of the teachings of McDevitt et al., which is provided at page 3 of the instant Office Action, McDevitt et al. disclose that “the blank microspheres provide a reference signal to which multiple different signals can be compared thereby allowing simultaneous evaluation of multiple chemically distinct analytes” (see instant Office Action at page 3, citation omitted). This is the definition of a negative control. The blank particle, at a known location, is monitored to determine a background emission from a particle possessing no test agents. This background emission can then be subtracted from emissions produced by particles having test agents associated therewith. If the emission produced from the blank (negative control) particle is similar in magnitude to the emission produced from particles having test agents associated therewith, the researcher becomes apprised that all emissions produced by particles on the array are suspect. Such valuable information, however, can be obtained only if the location of the blank (negative control) particles is known. Because McDevitt et al. only disclose using blank particles as negative controls and because the location of the particle must be known for the particle to function as a negative control, McDevitt et al.

cannot teach or suggest the random distribution of blank microspheres at the first and second assay locations as recited by the above-rejected claims.

Additionally, in view of the teachings of McDevitt et al., a skilled artisan would not be motivated to randomly distribute the blank microspheres disclosed by McDevitt et al. on an array disclosed by Walt et al. with any reasonable expectation of success. Applicants submit that a skilled artisan would place a particle used as a negative control at a known location on an array since the purpose of the negative control is to provide assurance that signals being generated on the array are not false positives. If blank beads are randomly distributed on an array, then the researcher will not know the location of the blank particles on the array. Without such knowledge, the particles are not effective as negative controls since the researcher would not know whether the lack of a signal at a particular position is by error or by design. As such, there is neither a motivation to make nor a reasonable expectation of success in making the combination asserted by the Examiner.

In view of the foregoing remarks, Applicants respectfully submit that the combination of Walt et al. and McDevitt et al. does not teach or suggest all of the elements of any of the above-rejected claims. Furthermore, a skilled artisan would not be motivated to randomly distribute blank particles on the arrays disclosed by Walt et al. since the skilled artisan would not expect randomly distributed blank beads to function as negative controls, which is the purpose for using blank particles as set out by McDevitt et al. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 60, 66-71, 77-83, 89-96, 103, 104, 106-117, 127, 129 and 131-141 as allegedly obvious over the combination of Walt et al. and McDevitt et al.

Second allegation of obviousness

In connection with the second allegation of obviousness, Applicants argued in their response filed August 27, 2009 that the combination of Walt et al. and Seul et al. does not teach or suggest, among other things, the random distribution of blank microspheres at the first and second assay locations as recited by the above-rejected claims. In particular, Applicants argued that Seul et al. disclose only the random distribution of particles with respect to the chemical identity of the particle, which is not sufficient to teach random distribution of a particle that does

not have a chemical identity, that is, a blank microsphere. In the instant final Office Action, the Examiner responded to Applicants' arguments as follows:

Applicant acknowledges that Seul uses blank microspheres, but argues that the reference teaches the microspheres are random with respect to chemical identity but spatially ordered. From this, Applicant asserts that a skilled artisan using blank microspheres to increase spacing would view ordered including of blank microspheres as a necessary method for achieving regular spacing between all of the encoded microspheres. The argument has been considered but is not found persuasive. As Applicant notes, the microspheres of Seul are random at least with respect to chemical identity. Furthermore, as cited in the Office Action, Seul specifically teaches and illustrates that randomly distributed microspheres (Fig. 28). While the resulting arrangement may be spatially ordered (e.g. 4X4 matrix), the microspheres of Seul are randomly distributed (Column 9, lines 17-20). Applicant's argument regarding the skilled artisan's use of blank microspheres is not supported by any factual evidence of such an interpretation. Therefore, the assertion is deemed unsupported arguments of counsel (see instant Office Action at pages 8-9).

Applicants have duly considered the Examiner's response to their arguments filed August 27, 2009 but maintain their position that the combination of Walt et al. and Seul et al. does not teach or suggest the random distribution of blank microspheres at the first and second assay locations as recited by the above-rejected claims. The relevant portions of Seul et al. that are cited in the Examiner's Office Action of February 27, 2009 and the instant final Office Action are column 25, lines 2-21 and Figure 28. First, the paragraph encompassing lines 2-21 of column 25 of Seul et al. is reproduced as follows:

In contrast to all prior art methods, the present invention provides a novel method to create heterogeneous panels by in-situ reversible formation of a planar array of chemically encoded beads in solution adjacent to an electrode. The array may be

random with respect to chemical identity but is spatially ordered. This procedure offers several advantages. First, it is reversible so that the panel may be disassembled following the binding assay to discard beads scoring negative. Positive beads may be subjected to additional analysis without the need for intermediate steps of sample retrieval, purification or transfer between containers. Second, the panel is formed when needed, that is, either prior to performing the actual binding assay, or subsequent to performing the assay on the surface of individual beads in suspension. The latter mode minimizes potential adverse effects that can arise when probes bind to planar target surfaces with a high concentration of target sites. Third, to accommodate optical analysis of individual beads, interparticle distances within the array may be adjusted by field-induced polarization or by the addition of inert spacer particles that differ in size from the encoded beads. FIG. 7 shows the use of small spacer beads 72 for separating encoded beads 74. As shown, the spacing of beads 74 is greater than the spacing of comparable beads in FIG. 4*b*. Finally, UV-mediated oxide regrowth, as provided by the present invention, readily facilitates the embedding of a grid pattern of selected dimension into the substrate to ensure the formation of small, layout-preserving subarrays in the low-impedance fields of the grid (see Seul et al. at column 24, line 66 to column 25, line 27).

Figure 28, which is discussed at column 44, lines 43-67 of Seul et al., is also reproduced as follows:

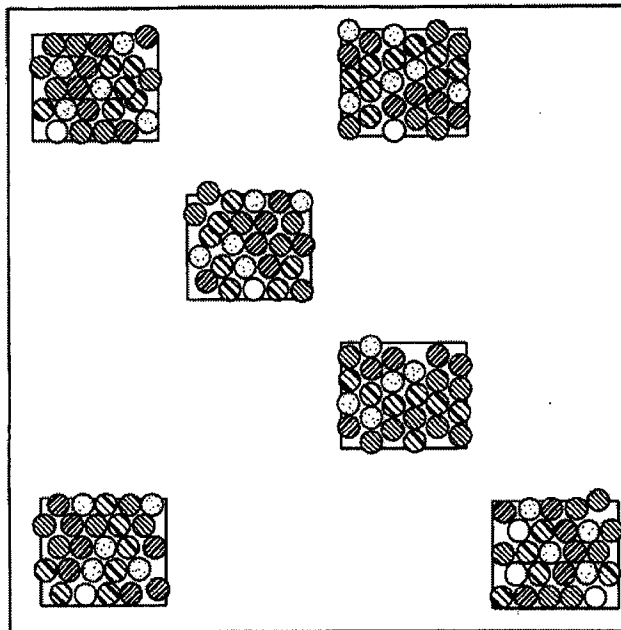


FIG. 28

(see Seul et al. at Figure 28).

Applicants have carefully reviewed Seul et al., and in particular, the passages and figures mentioned above. Nevertheless, Applicants can find no teaching or suggestion of randomly distributing blank microspheres at said first assay location and at said second assay location as recited in the above-rejected claims. Seul does state that inert spacer beads can be used to adjust interparticle distances (see Seul et al. at column 25, lines 15-22). With respect to Figure 28, Applicants do not see any description of blank microspheres. Applicants have reviewed the passages of Seul discussing Figure 28 and could find no description of blank microspheres. As such, it seems that the only disclosure related to blank microspheres appears at column 24, line 66 to column 25, line 27. As discussed in Applicants' previous response filed August 27, 2009, Seul et al. specifically state that "[t]he array may be random with respect to chemical identity but is spatially ordered." (see Seul et al. at column 25, lines 2-4, emphasis added). This line is deserves some attention. Here, Seul et al. state that randomness has at least two separate aspects. The first aspect is randomness with respect to chemical identity. The second aspect is randomness with respect to spatial distribution. Seul et al. plainly state that the disclosed array is

“random with respect to chemical identity but is spatially ordered” (see Seul et al. at column 26, lines 3-4). Blank microspheres have no chemical identity. This is self evident since these microspheres lack a chemical agent. Seul et al. disclose that beads can be randomly distributed on an array, but only with respect to chemical identity. Because blank microspheres do not have a chemical identity, they cannot be randomly distributed with respect to chemical identity, which is the only type of random distribution disclosed by Seul et al. As such, no combination of Walt et al. and Seul et al. disclose randomly distributing blank microspheres at said first assay location and at said second assay location as recited in the above-rejected claims.

In addition to the foregoing, it should be pointed out that Seul et al. only discuss using blank beads so as to increase spacing between individual agent-bearing beads that are present in bead clusters on contiguous planar arrays. A skilled artisan would not take the disclosure of Seul et al. as a suggestion to add blank microspheres to the device of Walt et al., which does not relate to contiguous arrays of bead clusters. Furthermore, even if it is assumed, *arguendo*, that a skilled artisan would be motivated to make such a combination, the artisan would have no reasonable expectation of success in obtaining a regular spacing between beads containing the chemical agents if the blank beads were randomly distributed on the array. As such, the art of record does not show that any of the above-rejected claims is obvious over the combination of Walt et al. and Seul et al.

In view of the foregoing remarks, Applicants respectfully submit that the combination of Walt et al. and Seul et al. does not teach or suggest all of the elements of any of the above-rejected claims. Furthermore, Applicants submit that a skilled artisan would not be motivated to utilize the blank particles disclosed by Seul et al. on the arrays disclosed by Walt et al. and that a skilled artisan would not have a reasonable expectation that such a combination would be successful because random distribution of blank beads into a bead cluster would not achieve regular spacing between beads. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 60, 66-71, 77-83, 89-96, 103, 104, 106-117, 127, 129 and 131-141 as allegedly obvious over the combination of Walt et al. and Seul et al.

Third allegation of obviousness

In connection with the third allegation of obviousness, Applicants argued in their response filed August 27, 2009 that no combination of the art of record teaches or suggests, among other things, the additional limitation that certain pluralities of depressions have microspheres from both populations of microspheres associated therewith. This additional limitation is recited by dependent claims 95, 96 and 112-117 as well as dependent claims 134-141. In the instant final Office Action, the Examiner responded to Applicants' arguments as follows:

Applicant further asserts that claims 112-117 provide further basis for patentability by requiring that blank microspheres are located in the same depressions as microspheres comprising the bioactive agent. The argument has been considered. However, it is maintained that the references teach all the elements of the claims. The independent claims require random distribution of a second population of microspheres wherein the second population comprises blank microspheres. Thus, the second population is not limited to only blank microspheres. Claims 112-117 defines the depressions of the first and second assay locations as having microspheres from both the first and second microspheres populations. As discussed above, all the of the references teach random distribution of microsphere populations and Seul specifically illustrates both populations in both assay locations (see instant Office Action at page 9, citation omitted).

After having carefully reviewed the Examiner's response to Applicants' arguments filed August 27, 2009, Applicants maintain their position that no combination of the cited art teaches or suggests either of the following claim limitations:

- "said second plurality of depressions have microspheres from said first population of microspheres and said second population of microspheres associated therewith" (for example, see claim 95)

- “said first plurality of depressions have microspheres from said first population of microspheres and said second population of microspheres associated therewith” (for example, see claim 96)

The Examiner maintains the rejection of claims 95, 96, 112-117 and 134-141 because the a combination of Walt et al., McDevitt et al. and/or Seul et al. allegedly discloses all the elements of the claims. As set forth in the quoted section above, the Examiner asserts that each of the “independent claims require random distribution of a second population of microspheres wherein the second population comprises blank microspheres. Thus, the second population is not limited to only blank microspheres. Claims 112-117 defines the depressions of the first and second assay locations as having microspheres from both the first and second microspheres populations. As discussed above, all of the references teach random distribution of microsphere populations and Seul specifically illustrates both populations in both assay locations (Fig. 28, column 44, lines 43-67)” (see instant Office Action at page 9, emphasis retained). Applicants believe that the wording of the last two sentences is particularly relevant here. Specifically, Applicants would like to point out that the Examiner correctly describes the claim limitations at issue as reciting “depressions of the first and second assay locations as having microspheres from both the first and second microspheres populations” (see instant Office Action at page 9, emphasis added). However, in the second sentence of these last two sentences, the Examiner alleges that all of the cited art teaches “random distribution of microsphere populations and Seul specifically illustrates both populations in both assay locations (Fig. 28, column 44, lines 43-67)” (see instant Office Action at page 9, emphasis added). Even if it is assumed, *arguendo*, that all of the cited art teaches “random distribution of microsphere populations and Seul specifically illustrates both populations in both assay locations” as suggested by the Examiner, such teaching is simply insufficient to disclose that depressions within the assay locations include microspheres from both the first and second populations. As such, Applicants must maintain that no combination of the art of record discloses all of the elements of any of claims 95, 96, 112-117 or 134-141.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 95, 96, 112-117 and 134-141 as obvious under 35 U.S.C. § 103(a).

Rejection of claims 65, 67, 70, 76, 78, 81, 88, 90, 93, 101, 102, 105, 126, 128, 130 and 133 under 35 U.S.C. § 103(a)

The Examiner rejects claims 65, 67, 70, 76, 78, 81, 88, 90, 93, 101, 102, 105, 126, 128, 130 and 133 as allegedly obvious over Walt et al. in view of McDevitt et al. and/or Seul et al. further in view of U.S. Patent No. 6,232,066 (Felder et al.). The Examiner applies the combination of Walt et al., McDevitt et al. and Seul et al. essentially as described above and applies Felder et al. for the alleged disclosure of array locations separated by gaskets. In particular, the Examiner asserts that Walt et al. “desire[] segregation of microsphere subpopulations to provide spatial encoding” and that a skilled artisan would have been motivated to combine the above-cited disclosures, with a reasonable expectation of success, in order to “provide for fluidically controlled multi-sample testing without cross contamination between adjacent regions.”

Applicants submit that claims 65, 67, 70, 76, 78, 81, 88, 90, 93, 101, 102, 105, 126, 128, 130 and 133 are not obvious over any combination of the above-cited references. As discussed above, Applicants submit that the combination of Walt et al., McDevitt et al. and/or Seul et al. does not teach or suggest all of the elements of any of the currently pending independent claims. The Felder et al. reference does not even mention blank microspheres, and thus, it does not remedy this deficiency. Furthermore, for at least the reasons discussed above, a skilled artisan would not be motivated to combine the disclosure of Walt et al. with those of McDevitt et al. and/or Seul et al. with any reasonable expectation of success so as to arrive at the subject matter set forth in the currently pending independent claims. The Felder et al. reference does not provide such motivation or reasonable expectation of success. Accordingly, no combination Walt et al., Felder et al., McDevitt et al., and/or Seul et al. renders any of the above-rejected claims obvious.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 65, 67, 70, 76, 78, 81, 88, 90, 93, 101, 102, 105, 126, 128, 130 and 133 under 35 U.S.C. § 103(a).

Application No.: 10/638,173
Filing Date: August 6, 2003

New claims 142-155

In addition to the foregoing arguments, Applicants take this opportunity to present additional claims drawn to composite arrays and methods of making such arrays. Applicants submit that these new claims are patentable for at least the reasons discussed above. As such, Applicant respectfully request that the Examiner fully consider the patentability of new claims 142-155 in connection with the above remarks and the limitations recited these claims.

Co-Pending Application of Assignee

Applicants wish to draw the Examiner's attention to co-pending, co-owned U.S. Patent Application No. 10/856,039. The Examiner may wish to consider the currently pending claims and/or prosecution history of that application.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.


Application No.: 10/638,173
Filing Date: August 6, 2003

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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